

PHYSIOLOGICAL AND PSYCHOLOGICAL RESULTS OF SPACE FLIGHT

In trying to predict how a human crew might perform in the novel environment of space flight, flight physicians and researchers of the 1950s speculated that microgravity and space flight itself would present significant challenges to the human body (1). They hypothesized that the combination of acceleration during launch, weightlessness itself, and heavy deceleration during entry would be incapacitating; at the very least, they expected the bodily systems that relied on gravity-based cues to function improperly or not at all. Given this grim forecast, the initial focus of human space flight was to demonstrate that humans could indeed survive space flight and the subsequent return to Earth's gravity.

In the space of a few decades, human space flight has evolved considerably from the first flights proving that humans could endure microgravity. Since those flights, the Russian program has maintained a crewed space station in orbit for more than a decade and American astronauts have shepherded the orbital Shuttle through over 100 missions. An intrinsic, even critical, component of this evolution has been to define and overcome the biomedical challenges of space flight. Refinement of technology and protocol has freed crewmembers from operational tasks and allowed them to devote more time to biomedical investigations, including validation of appropriate countermeasures. Although the complexity of the adaptive response requires ongoing research, numerous studies have accomplished significant inroads in both fundamental and applied knowledge.

THE SPACE FLIGHT ENVIRONMENT

While aviators of high-speed aircraft had considerable experience flying in conditions similar to those of space flight, the first astronauts and cosmonauts were required to function—eat, drink, communicate, and move—for extended periods of time in a novel and complex environment. Early biomedical studies demonstrated that the combined factors of space flight did exact a toll on the physical performance and psychological health of crewmembers. Furthermore, the first crewmembers and flight engineers realized that space flight was really the sum of several complex factors, only one of which was microgravity. In sum, the success of a mission is driven by a number of parameters—crew performance, crew health, the internal environment, and the external environment—that together represent the biomedical challenges of space flight.

External

In orbit, a spacecraft moves around the Earth in a constant state of free fall that produces microgravity. Because all organisms on Earth have evolved and developed in the presence of gravity, microgravity requires adaptive changes in the human crew; these are initiated immediately upon exposure to microgravity, some of which continue for the course of the mission. At the most basic level, microgravity may be considered an environmental stimulus that induces a cascade of regulatory mechanisms in the human body. The results of these mechanisms are adaptations, changes in physiologic function and structure that alter health and performance in flight and post flight if altered conditions continue.

Although the most conspicuous characteristic of the space flight environment is reduced gravity, a number of other factors contribute to its biomedical effects on humans. Primarily, space is a hostile environment for humans. It is distinguished by profound fluctuations in temperature ranging from 220K in the stratosphere to 1000K in the thermosphere (2) [refer to II.2, Physics of the Near-Earth Environment], a lack of a breathable atmosphere due to a near-

perfect vacuum, and a number of constant and intermittent radiation events. Data collection and analysis during a mission focuses on temperature extremes, unexpected radiation events, baseline radiation exposure levels, and orbital debris.

The radiation environment is comprised of several sources of ionizing radiation, a general term that encompasses particles capable of altering molecular electrons upon contact: solar energetic particles emitted during solar flares, trapped particles in the Earth's magnetic field, and galactic cosmic radiation (3). Although each of these sources consists of various types of space radiation particles, the most significant barriers to mitigating radiation exposure are

- 1) an incomplete understanding of the detrimental effects caused by ionizing radiation, and
- 2) an inability to fully predict and model radiation events in time to protect a space faring crew.

Presently, crew and spacecraft interior are monitored by a series of passive and active dosimeters that are analyzed post flight, while ground-based monitoring can warn of impending solar flares so that the mission can be abbreviated. With the emphasis on increasing duration missions, however, the debilitating long-term effects of radiation will require both enhanced methods of monitoring and increasingly accurate modeling and prediction methods (4).

Internal

The human-rated spacecraft must both protect the crew from the hostile external environment and provide the resources necessary to support human life and work [refer to I.10, Spacecraft Designed to Carry People]. The design and performance of such spacecraft has evolved considerably, from the first space capsules to the "shirt-sleeve" environment of the International Space Station. Common to all spacecraft environments, however, is the requirement for appropriate air, water, temperature and pressure with appropriate consideration for the human factor in design and performance; that is, the environment must be precisely monitored and maintained using a minimum of resources including power, mass, crew time, and noise (5).

The spacecraft environment itself provides additional challenges to crew health and safety. A majority of these constraints result from the physical environment of orbital space flight. Not only are the crewmembers expected to live in a confinement far distant from friends and family, but they are subjected to extreme scrutiny and pressure to complete their work in a timely and consistent manner (6). This stress and isolation is compounded by the fact that a sunrise or sunset occurs every 90 minutes in low Earth orbit. While initially disconcerting to crewmembers, altered dark-light cycles have a significant physiological on the quality and quantity of sleep. The sum of these challenges, both mental and physical, can exact a considerable toll on crewmembers unless they have appropriate support from ground personnel, sufficient personal time and space, and flexible work/rest schedules. Numerous analogue environments, including extended bed-rest and Antarctic wintering-over expeditions, have been explored to understand the cumulative effects on human performance and psychosocial health. Likewise, long-duration space flights have revealed the substantial influence of these factors on mission success.

BIOMEDICAL CHALLENGES

The systems of the human body work in a complex concert to sense and respond to the surrounding environment, be it the normal gravity environment of Earth or the close quarters of spacecraft in low-Earth orbit. While the relationships between these various systems have yet to

be fully elucidated, significant progress in understanding the human response to space flight has been made. Progress in fundamental and applied knowledge comes from both ground-based biomedical studies, including analogs such as bed-rest or centrifugation, and from space-based investigations that trace their beginnings back to the first human space flights. Table 1, Changes Associated with Space Flight, represents the sum of our current knowledge about the most significant challenges to crew health, performance, and safety during space flight.

Because of the complexity and individual nature of human adaptation to space flight, changes are often considered on a systemic basis. While this approach is useful for understanding system-specific alterations, it does not fully characterize the effects of living and working in the space flight environment. As a result, more recent studies have focused on whether crewmembers maintain appropriate levels of functional performance, the ability to perform key activities such as intra- and extra-vehicular activity or emergency egress, during or following long-duration space flight. Aerobic capacity, a measure of how much oxygen is consumed during a single bout of maximal exercise, reflects the integrated performance of the cardiovascular, nervous, and musculoskeletal systems. As illustrated in Figure 1, aerobic capacity is diminished by space flight but does show an immediate improvement towards preflight levels upon return to Earth.

Cardiovascular Deconditioning

The human cardiovascular system has evolved in the presence of gravity as an intricate network of vasculature fed by the powerful cardiac muscle. This vasculature is composed of both muscular arterial vessels that supply oxygenated blood to tissue and non-muscular venous vessels that return blood to the heart. Baroreceptors and stretch-sensitive receptors monitor the critical parameter of blood pressure in vessels throughout the body. On Earth, simple motions such as sitting, standing, or reclining result in significant and rapid responses to the changes in gravitational force imposed upon the body.

Unlike the limited and short-lived changes in gravity encountered on Earth, microgravity presents a challenge to the cardiovascular system that is generally stabilized by the fifth week of flight. In even longer Soviet space flights (three months to one year or more), a slight increase in heart rate has been noted, particularly toward the end of the mission (7). Nevertheless, cardiovascular deconditioning appears to be a self-limiting phenomenon that does not continue to decline during the flight and does improve upon return to Earth. Cardiovascular deconditioning represents an appropriate adjustment of the cardiovascular system to a new environment, in which the gravitational load placed on the heart is considerably less than on Earth.

During flight a host of adaptive mechanisms occur to the cardiovascular system. Fluid pooling no longer occurs in the lower extremities, but is instead localized to the upper body. Physically, this shift is revealed by facial edema, sinus congestion, and decreased calf girth and leg volume ("bird legs"). This shift is perceived as excess fluid, which in turn affects a series of immediate but long-lasting changes. An immediate decrease in plasma volume occurs, in addition to a more gradual loss of red blood cell mass of approximately 10% (8). This condition is primarily attributed to a decrease in the circulating blood volume. Systematic investigations have proven difficult because of individual differences in diet, sleep patterns, exercise, medications, and fluid intake associated with various space missions. Recent cardiovascular studies have focused on

- establishing a normative database of cardiovascular changes that result from space flight,
- determining the mechanisms that underlie these cardiovascular changes, and

- Evaluating potential countermeasures.

Cardiovascular deconditioning becomes a medical problem only after crewmembers are subjected to acceleration forces during reentry or upon return to the constant 1-g stress on Earth. As early as the American Gemini program, cardiovascular deconditioning was documented in 100% of the crewmembers. One component of this deconditioning is orthostatic intolerance, the inability to function effectively against gravitational stress, such that simple actions like sitting and standing may result in episodes of weakness, dizziness, or fainting. A standard measure of orthostatic intolerance is the stand test, in which recently returned crewmembers are asked to stand upright for several minutes after a period of reclining; by monitoring blood pressure and heart rates during this functional challenge, researchers can associate significantly altered arterial pressures with adaptation to space flight and the gravitational forces of landing. As shown in Figure 2, approximately 20% of the crewmembers showed altered levels of systolic and diastolic pressure following flight. Depending on the duration of the space flight and the amount of exercise performed in flight, the return of cardiovascular function to preflight values may require as long as 1 month.

Neurosensory Disturbances

The central nervous system (CNS) controls both perception of and interaction with the environment. Sensory systems, including the visual, vestibular, and proprioceptive organs, respond to environmental stimuli and supply a constant flow of input to the CNS. In conjunction with a visual image of surroundings, the vestibular and proprioceptive systems supply additional information relating to orientation, balance, and limb location. The CNS processes this set of information and then directs the musculoskeletal systems for movement and interaction with the environment. Each step in this intricate process is contingent upon a constant inflow of information about the surrounding environment. In the microgravity of space flight, however, the CNS must not only adapt to a loss of sensory and proprioceptive input, but it must also respond to reduced muscular capacity, including functional and structural changes in muscle tissue. Adaptation to unexpected or even absent sensory information is neither an instantaneous nor a constant process; thus identifying the mechanisms responsible and the appropriate countermeasures is somewhat of a challenge. Neurosensory adaptations have traditionally been difficult to measure, but fortunately are evidenced through inflight and postflight changes in crew performance.

Clinically, the most important vestibular disturbance associated with space flight is space motion sickness (SMS). The classic model for the onset of SMS is found in a description provided by the Soviet cosmonaut Titov. For a brief period after transition into orbit, Titov felt that he was flying upside down. This was followed by dizziness associated with head movements. Some time between the fourth and seventh orbits, or six or more hours into the flight, he became nauseated and ill. This was the first recorded instance of space motion sickness.

As Titov noted, most crewmembers do experience a sensation of bodily inversion, which soon passes but could recur with rapid movement. More susceptible individuals, however, develop a full host of SMS symptoms (9). Russian demographics suggest that SMS affects 30-40% of cosmonauts, while American astronauts report slightly higher occurrences (70%). SMS occurs early in the mission, typically within the first 3 days. Symptoms range from minimal discomfort to nausea and vomiting, in rare cases accompanied by pallor and sweating. Head and body movements tend to worsen the discomfort. When the symptoms are severe, crew

performance can be affected and mission efficiency severely compromised. During the Apollo IX mission, for example, certain crew activities were delayed by 24 hours due to space motion sickness.

The medical basis for space motion sickness is not fully understood, partly because the phenomenon can be studied effectively only during space flight. Guedry *et al.* (10) summarize studies of motion sickness in flight and on the ground, in which the most plausible explanation for neurosensory changes is the “sensory conflict” hypothesis. According to this concept, the usual sensory inputs to the vestibular receptors of the inner ear are no longer present in microgravity, causing altered processing of sensory information and ultimately resulting in altered motor responses.

Both the Russian and American human space flight programs recognize the complex interactions within and between the sensory, nervous, and muscular systems, and are continuing research into this area.

Musculoskeletal Alterations

An integrated response from the skeletal, muscular, connective tissue, and nervous systems permits movement in the 1 g environment. This response is predicated on the fact that certain directional forces will have to be overcome in order to complete ordinary tasks, like lifting an object or walking down stairs. In the microgravity environment, however, these directional forces are altered; the result is a cascade of functional and structural changes to the physiologic systems that control locomotor tasks. Collectively, these changes yield reductions in strength, power, and endurance that ultimately influence crewmembers’ ability to perform routine motor activities (Table 2). The changes are ordinarily indicated in flight by a progressive decrease in total body mass, leg volume, and muscular strength. As weight-bearing muscles and bones adapt to the microgravity environment, several symptoms are manifested. Disturbances in postural and motor coordination, locomotion function, and equilibrium can be seen, and alterations in proprioceptor activity and spinal reflex mechanisms occur. Although all of these changes appear to be dependent, at least to some extent, on flight duration, they have been reversible, and no adverse sequelae have been reported thus far.

A primary indicator of changes in bone and muscle mass is body mass: in-flight weight losses of 3 to 4% were seen in association with early, short-duration space flights. With the advent of longer missions, most of weight loss took place during the first three to five flight days, with a much more gradual decline thereafter (11). This finding suggests that a significant part of the initial change in body mass is due to the loss of fluids, either through diuresis or decreased thirst and fluid intake, and that subsequent losses are due to metabolic imbalances and/or muscle atrophy. The changes appear to be self-limiting, with the largest weight losses recorded (6 to 7 kg) being independent of mission duration. In more recent long-duration space missions, where adequate caloric intake and physical exercise have been maintained by some of the crewmembers, actual weight gains have been reported. Such weight gains probably reflect an overall increase in fatty tissue which was more than sufficient to offset losses of muscle tissue. In any event, body mass lost in flight is rapidly regained in the postflight period.

Muscle Atrophy

Microgravity and the loss of nominal gravitational loads produce a number of structural and functional changes in skeletal muscle. These changes are most readily apparent in the postural or antigravity muscles, such as the gastrocnemius and the muscles of the back and the neck. Skeletal muscles exhibit numerous alterations in strength and endurance properties,

including force- and power-generating capacities, shortening and relaxing rates, neural activation patterns, protein expression, and metabolic utilization profiles. Concomitant to these muscular changes, connective tissues undergo similar atrophy and functional alteration. At the molecular level, both slow-twitch and fast-twitch muscle fibers are affected. The process of functional and structural change is progressive and can be controlled to some extent by high caloric intake and intensive strength exercises.

Evidence for the deterioration of muscle during space flight comes from several sources. In-flight measurements of leg volume (Figure 3) show an initial rapid decrease that can be attributed to the headward fluid shift, and is followed by a gradual recovery. Postflight biostereometric measurements of Skylab astronauts demonstrated more general losses of volume from the abdomen downward, although losses in the abdomen and buttocks were attributed to the loss of fat (12). Postflight urinary analyses reveal in-flight increases in the excretion of a number of metabolites associated with muscle breakdown, such as nitrogen, potassium, creatine, and amino acids. Metabolic balance studies and electromyographic analyses of muscular activity further substantiate the deterioration of muscle function during space flight.

Bone and Mineral Changes

The removal of muscular forces and weight from bones, as occurring in bed-rest or having a limb in a cast, causes a loss of bone mineralization, known as disuse osteoporosis. During space flight, crewmembers experience a form of musculoskeletal disuse in which levels of bone mineral are decreased. Early studies of bone mineral changes using x-ray densitometry suggest that large amounts of bone may be lost during relatively brief periods of space flight and countermeasures to this loss are mandatory for long-duration missions (13). The 12 crewmembers who participated in the Gemini 4, 5, and 7 and Apollo 7 and 8 missions averaged 3.2% post-flight losses of bone density from the calcaneus (heel bone) as compared with preflight baseline values. Some losses also were observed from the radius and ulna after these early flights.

In sum, these changes to the systems that direct locomotion mean that crewmembers are at risk for increased falls, bone fractures, and limited mobility – conditions which at a minimum could make emergency egress a challenge.

Immunological Alterations

The immune system defends the body against any cell, substance, or organism not recognized as self. As such, it is affected by both environmental and physiological fluctuations that occur during space flight. Although results from some studies are contradictory, most studies conceded generally recognize an increase in the immune cells responsible for the immune response, known as leukocytes. More specifically, changes in the leukocyte population, particularly in the relative percentage of T and B lymphocytes, are altered compared to preflight levels. Lymphocytes from astronauts onboard Soyuz 6,7, and 8, Skylab 2, 3, and 4, and Salyut 4 exhibited poor response to mitogenic factors (14), the substances that induce the immune response. The cells, therefore, experience a reduced functional capacity in microgravity conditions.

The immune system, like other body systems, responds dynamically to varying conditions, which may explain why results from one study contradict those of others. Studies conducted as early as the Skylab program suggest that impaired immune function during spaceflight is closely linked to the endocrine system, and is particularly affected by corticosteroids and catecholamines (14); generally, this implies that changes in other regulatory

mechanisms could closely affect immune function. In addition, results from *in vitro* studies may not parallel results from *in vivo* studies, indicating that the physiologic environment plays an integral role in maintaining immunological integrity (15).

Stress has been shown in several studies to have a considerable influence on immunity. Astronauts experience psychological and physical stresses that may result in reactivation of latent viruses during space flight, potentially increasing the risk of infection among the crew. A study done on the amount of Epstein-Barr shedding pre-, in- and post flight showed that the virus, normally latent in most humans, was higher in samples taken before launch (16). Although these results from this study suggest that stress levels are higher before flight than during or after, reactivation of latent viruses, combined with depressed immune response in flight, pose a significant threat to missions, both short- and long-term.

Certainly, more studies need to be performed to better understand the intricate reactions of the immune system in space. Since immune function and activity are interdependent upon other systems of the body, there are implications for exploring countermeasures to mitigate the changes and for studying how pharmacological substances interact with the immune system in microgravity.

Hematologic, Fluid, and Electrolyte Changes

The cephalic shift of fluids in weightlessness, with the resulting decrease of circulating blood volume, is responsible for many of the physiologic changes that occur during adaptation to space flight conditions. As has been discussed, it directly affects the functioning of the cardiovascular system. It also has several effects on the composition of body fluids, especially blood (Table 1). The most significant hematologic changes involve a reduction in plasma volume, alterations in red blood cell (RBC) mass, and changes in the distribution of RBC shapes. From the time of the early Gemini and Vostok missions, a postflight decrease in total RBC mass has been observed in nearly all United States and Russian crewmembers. There is a gradual decrease, with losses averaging about 9% of the total RBC pool over the first 30 to 60 days in flight and values ranging from 2 to 21%. Cosmonauts participating in missions of 18 days to 6 months have shown postflight decrease in erythrocyte counts that returned to baseline values within 6 weeks (11).

The magnitude of the RBC loss does not appear to relate to mission length, except possibly in missions of 30 days or less. Changes in RBC are also accompanied by changes in the shapes of erythrocytes, although these alterations do not seem to affect crew health or function in flight and are rapidly reversed postflight. The weight of evidence now suggests that the loss of RBC mass is due, instead, to insufficient circulating erythropoietin in combination with neocytolysis, or a decreased survival rate of newly formed RBCs (8). To further complicate research and understanding, the decrease in RBCs is effectively masked by a simultaneous, rapid decline in plasma volume (4-16% from preflight values) such that the ratio of cells to plasma remains roughly normal.

The microgravity-induced fluid shift produces at least a transient increase in central blood volume. Research from ground-based bed rest studies suggests that the stretch receptors in the left atrium interpret this as an increase in total circulating blood volume, triggering a compensatory loss of water, sodium and potassium from the renal tubules. This is the first event in a series of fluid and electrolyte shifts that occur during the adaptation to weightlessness. So far, the early diuresis has been observed only in bed rest studies. It is difficult to demonstrate during space flight because of the problems involved in accurately documenting urine volumes

early in flight, and because water intake is usually reduced during the early stages of flight. Additional supporting observations included the observed in-flight increases in the urinary output of sodium, potassium and chloride, an in-flight decrease in antidiuretic hormone, and a reduced postflight excretion of sodium. Fluid retention has also been a consistent finding in cosmonauts after *Soyuz* flights, but excretion of potassium and calcium was found to increase.

Psychological Health

The space flight environment consists of many elements that, even if experienced separately, are both physically and mentally challenging. A confined living space, high public interest and visibility, isolation from family and friends, crowded or often unappealing spacecraft conditions, and requirement for strong group dynamics are but a few of the obstacles that cosmonauts and astronauts face. These factors are compounded by the physical fact that light/dark cycles are altered in orbit, which affects circadian rhythm and is evidenced by disrupted or insufficient sleep (17). The most prevalent psychological events as reported by crewmembers include: high levels of stress or tension, anxiety often demonstrated as annoyance at other crewmembers or ground support personnel, decreased levels of concentration, emotional instability including mood elevation or depression, and general fatigue.

As the potential for increasingly longer missions becomes feasible, psychological and behavioral support has become an element of both the American and Russian space medicine programs. Often, support takes the form of comparatively small changes in operations or scheduling that minimize crew requirements and permit crewmembers some flexibility in arranging their work/rest cycles. For example, astronauts have reported considerable improvements in outlook and performance when communications with family members or friends are provided on a regular basis.

TIMECOURSE OF ADAPTATIONS

The human body is exquisitely sensitive to changes in its surroundings and reacts to such changes with equal precision. Modest changes in the gravitational force, for example, result as a sitting person stands or a sleeping person awakens; these force differentials induce a host of regulatory or adaptive mechanisms, which ensure that blood consistently reaches all extremities. A more significant change to the gravitational environment—such as the microgravity of space flight—clearly challenges the body's homeostasis to a much greater extent.

The earliest orbital flights were conducted in small capsules and lasted only a few hours or days. Within these first human-rated spacecraft, the limited capacity for movement and the short exposure to microgravity meant that crewmembers mainly reported rapid onset adaptations (1). As mission duration has increased well beyond several days into months and even years, crews are now faced with further adaptive events and new physiologic challenges; adaptation to space flight is neither instantaneous nor consistent but instead is dependent upon individuals, mission duration, and operational activities (11). Despite these differences, all crewmembers returning from both short- and long-duration flights report two periods of adaptation that occur after the transition from one gravitational environment to another.

The first is experienced upon launch and entry into orbit. Some symptoms manifested early in the mission abate as the adaptation is resolved. The sensory conflict produced by the visual and vestibular systems is one example that is limited to the first three to eight days of a mission.

The return to Earth's gravity requires a second period of adaptation, which again presents a significant challenge to crew activity and safety. Orthostatic intolerance stems from the cardiovascular deconditioning and cephalic fluid shift that occur in response to microgravity; many crewmembers report presyncopal or syncopal episodes, that is dizziness or fainting, upon return to 1 g. Neuromuscular and neurovestibular adaptations produce postflight disequilibrium (including marked vertigo in some cases) and gait disturbances, both of which clearly limit coordinated maneuvers and interfere with nominal or contingency egress (10). Cosmonauts from long-duration Russian missions of eight months have required more than four weeks of rehabilitation to function normally (18). Physical performance also declines as a result of significant and sustained loss of bone and muscle mass, documented at 10-20% of preflight levels during extended-duration missions.

Other more obscure changes are observed only during specific functional tasks or after return to the 1 g environment. Bone and connective tissue changes, for example, begin as early as one week into a mission and can continue for more than a year. These changes are not typically apparent in flight, but are instead demonstrated upon return to Earth as locomotor problems, bone frailty, and increased risk of kidney stones (11).

CHALLENGES FOR EXPLORATION-CLASS MISSIONS

As human space flight programs continue beyond low Earth orbit, health monitoring and health maintenance through appropriate countermeasures will become more discrete and seamless in the spacecraft of the future. Crewmembers may well monitor their own medical status, evaluate environmental health, assess risks, and then direct the automatic correction or restoration of an anomaly. The opportunity for novel or previously unexplored countermeasure approaches, including artificial gravity, could well alter what are currently considered the most dire biomedical challenges of human space flight. The crew of the International Space Station and future spacefarers will be just as dependent as their forebears on the thorough understanding and mitigation of these challenges.

BIBLIOGRAPHY

- 1) Swenson L, Grimwood J, and Alexander C. *This New Ocean: A History of Project Mercury*. NASA SP-4201, Washington, DC: Government Printing Office, 1989.
- 2) Fazio G. "Vacuum, Temperature, and Microgravity" in S.E. Churchill, ed., *Fundamentals of Space Life Sciences*, Krieger Publishing Company, Malabar, Florida, 1997.
- 3) Badhwar G, "The Radiation Environment in Low-Earth Orbit," *Radiation Research*, Volume 148, 1997, S3-S10.
- 4) Straume T, and Bender, M, "Issues in Cytogenic Biologic Dosimetry: Emphasis on Radiation Environments in Space", *Radiation Research*, Volume 148, 1997, S60-S70.
- 5) Eckart P. *Spaceflight Life Support and Biospherics*. Microcosm Press and Kluwer Academic Publishers, Dordrecht, Germany, 1996.
- 6) Manzey D, Lorenz B, and Poljakov V. "Mental performance in extreme environments: results from a performance monitoring study during a 438-day spaceflight." *Ergonomics* 41(4):537-59, April 1998.
- 7) Goldberger A, Bungo M, Baevsky R, and Bennett B, Rigney D, Mietus J, Nikulina G, Charles J. "Heart rate dynamics during long-term space flight: report on Mir cosmonauts" *Am Heart Journal* 128(1):202-4, 1994.

- 8) Alfrey C, Rice L, Udden M, and Driscoll T. "Neocytolysis: physiological down-regulator of red-cell mass." *Lancet* 10;349 (9062):1389-90, 1997.
- 9) Graybiel A, Miller E, Homick J. "Equipment M131. Human vestibular function," Johnston R, and Dietlein L, Eds. *Biomedical Results From Skylab*. NASA SP-377. Washington, DC: Government Printing Office, 1977.
- 10) Guedry F, Rupert A, and Reschke M. "Motion sickness and development of synergy within the spatial orientation system. A hypothetical unifying concept." *Brain Research Bulletin* 15;47(5):475-80, 1998.
- 11) Sawin C. "Biomedical investigations conducted in support of the Extended Duration Orbiter Medical Project," *Aviation and Space Environmental Medicine*, Volume 70(2), pp.169-180, 1999.
- 12) Whittle MS, Herron R, Cuzzi J. "Biostereometric analysis of body form". Johnston R, Dietlein L, eds., *Biomedical Results from Skylab*. NASA SP-377, Washington, DC: Government Printing Office, 1977.
- 13) Nicogossian A, Pool S, Sawin C. "Status and Efficacy of Countermeasures to Physiological Deconditioning from Space Flight." *Acta Astronautica*, Vol. 36, No. 7, 1995, pp. 393-398.
- 14) Kimzey S. "Hematology and Immunology Studies," Johnston R, and Dietlein L, Eds. *Biomedical Results From Skylab*. NASA SP-377. Washington, DC: Government Printing Office, 1977.
- 15) Sherr, D. and Sonnenfeld, G, "Response of the Immune System to Spaceflight" in S.E. Churchill, Ed., *Fundamentals of Space Life Sciences*, Krieger Publishing Company, Malabar, Florida, 1997.
- 16) Payne, D, Mehta, S, Tying, S, Stowe, R, and Pierson, D. "Incidence of Epstein-Barr Virus in Astronaut Saliva During Spaceflight." *Aviation, Space and Environmental Medicine*, Volume 70, No.12, pp. 1211-1213, 1999.
- 17) Manzey D, and Lorenz B. "Mental performance during short-term and long-term spaceflight." *Brain Research and Brain Research Review* 28(1-2):215-21, 1998.
- 18) Vico L, Collet P, Guignandon A, Lafage-Proust M, Thomas T, Rehaillia M, and Alexandre C. "Effects of long-term microgravity exposure on cancellous and cortical weight-bearing bones of cosmonauts." *Lancet* 355(9215):1607-11, 2000.
- 19) Nicogossian A, Leach Huntoon C, and Pool S, Eds.. *Space Physiology and Medicine*, 3rd Edition. Philadelphia: Lea & Fibiger, 1994.

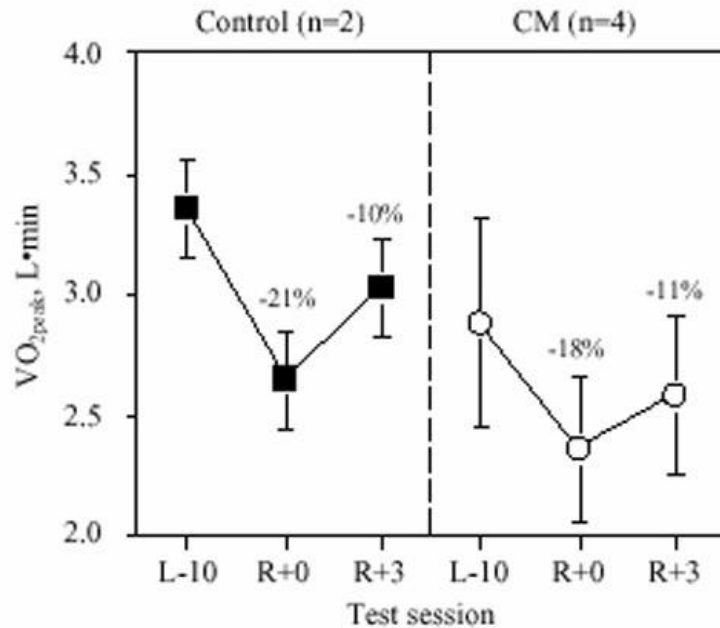


FIGURE 1. Aerobic capacity of crewmembers before launch (L-10days) and after flight (Return, Day 0 and Return, Day 3). Control subjects did not perform any exercise, while CM subjects performed exercises with an onboard cycle ergometer up to 48 hours before landing (from *Extended Duration Orbiter Medical Project*, 1997).

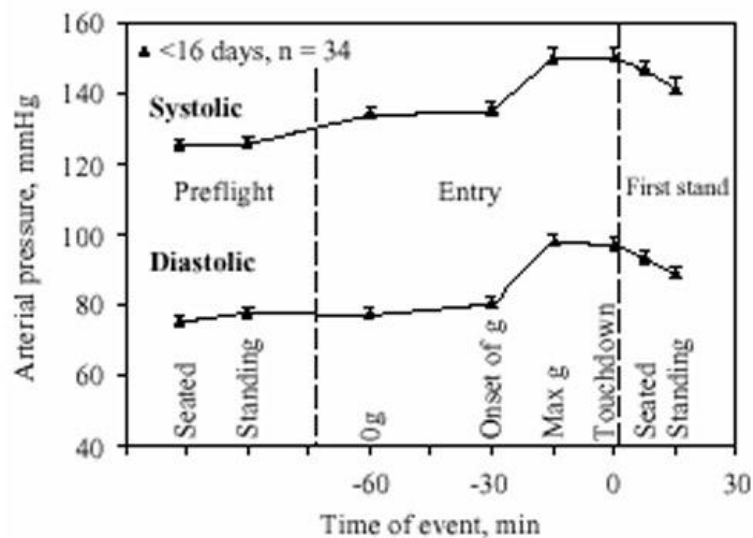


FIGURE 2. Systolic and diastolic pressure response of crewmembers to entry, landing, and egress shows altered reactions to the standard orthostatic challenge, the stand test (from *Extended Duration Orbiter Medical Project*, 1997).

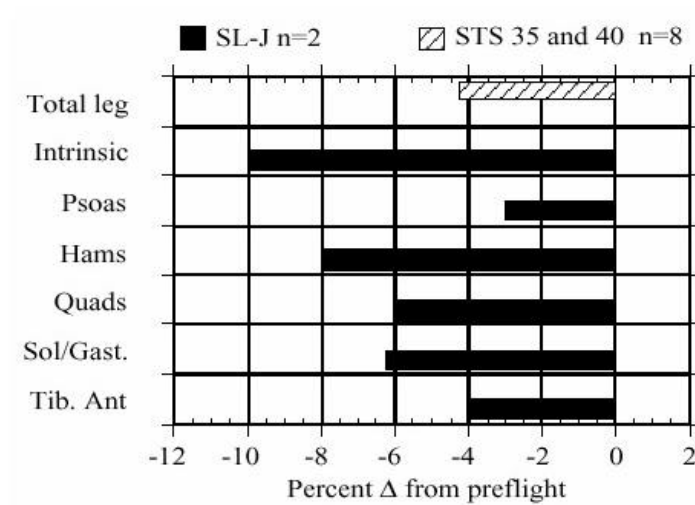


FIGURE 3. Percent decreases in volumes of various leg muscles, measured by magnetic resonance imaging, from three Extended Duration Orbiter Shuttle missions (from *Extended Duration Orbiter Medical Project*, 1997).

TABLE 1. A summary of the physiologic changes associated with human space flight (from Nicogossian, Huntoon, and Pool (19)).

Physiologic Measure	Change Associated with Short Space Flights (<2 weeks)	Change Associated with Long Space Flights (>2 weeks)
Cardiovascular System		
Resting heart rate	↑↓ in flight with peaks during launch and entry	Normal or slight ↑
Resting blood pressure	↔	Diastolic blood pressure ↔ or ↓
Total peripheral resistance	↓; no ↑ at landing despite ↓ stroke volume and ↑ heart rate	Tendency toward ↓
Stroke volume	↑ by as much as 60% but compensated by ↓ heart rate	
Exercise capacity	↔ or ↓ ≤ 12% after flight; increased HR for same O ₂ consumption; efficiency ↔	Submaximal exercise capacity ↔
Body Fluids		
Total body water	3% ↓ by flight day 4 or 5	
Plasma volume	↓ in flight and postflight	
Hemoglobin	↔ or slightly ↑ after flight	↑ (first in-flight sample) followed by slow ↓
Red blood cell (RBC) mass	↓ after flight (approximately 9%); sustained at least 2 weeks	↓ approximately 15% during first 2-3 weeks; recovery begins after 60 days and is independent of mission duration
Plasma lipids	↓ cholesterol and triglycerides in flight	
Plasma glucose	↓ during and immediately after flight	↓ first 2 months, then leveled off
Serum/plasma electrolytes	↑ K and Ca in flight; ↓ Na in flight; ↓ K and Mg postflight	↓ Na, Cl, and osmolality; slight ↑ K and PO ₄
Urine electrolytes	Post flight ↑ in Ca, creatinine, PO ₄ and osmolality; ↓ in Na, K, Cl, and Mg	↑ osmolality, Na, K, Cl, Mg, Ca, and PO ₄ ; ↓ in uric acid excretion
Insulin		↓

Urine volume	Post flight ↓	↓ early in flight
Sensory Systems		
Gustation and olfaction	Subjective and varied experience; no impairments noted	Same as shorter missions
Vision	Intraocular tension ↑ in-flight and ↓ at landing; post flight ↓ in visual field, visual motor task performance and contrast discrimination; ↔ in-flight contrast discrimination or distant and near visual acuity; dark-adapted crews reported light flashes with eyes open or closed; retinal blood vessels constricted postflight	Light flashes reported by dark-adapted subjects; frequency related to latitude
Vestibular	40-70% astronauts/cosmonauts exhibit in-flight neurovestibular effects, including immediate reflexive motor responses and space motion sickness; motion sickness symptoms appear early in flight and subside or disappears in 2-7 days	In-flight vestibular disturbances are same as for shorter missions; cosmonauts have reported occasional reappearance of illusions during long-duration missions.
Musculoskeletal System		
Height	Slight ↑ (~1.3 cm/ 0.5 in) during first week in flight, with 1 day recovery to baseline	↑ during first two weeks in flight by a maximum of 3-6 cm (1.2-2.4 in); stabilizes thereafter
Mass	Post flight weight ↓ average 3.4%; about 2/3 is due to water loss and the remainder due to lean body mass and fat	In-flight weight losses average 3-4% during first 5 days and are probably due to loss of fluids; thereafter, weight ↑ or ↓ for the remainder of the mission and is related to metabolism
Extracellular fluid volume	↓ 15% on flight day 2	
Total body volume	↓ postflight	Center of mass shifts headward
Muscle strength	↓ during and after flight, with 1-2 weeks recovery to baseline	
EMG analysis	Post flight EMGs from gastrocnemius suggest ↑ susceptibility to fatigue and ↓ muscular efficiency; EMGs from arm muscle ↔	
Bone density	Os calcis density ↓ postflight; radius and ulna show variable changes, depending upon method	

Calcium balance	↑ negative Ca balance in flight	Excretion of Ca ↑ during first month of flight; fecal Ca excretion ↓ until day 10 then ↑ continually throughout mission; Ca balance becomes ↑ negative throughout mission
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↔ unchanged
 ↓ decrease
 ↑ increase
 N/A not measured

TABLE 2. Mean strength performance of skeletal muscle on landing versus preflight (n=17) during concentric and eccentric (extension) motions of selected muscle groups (from *Extended Duration Orbiter Medical Project*, 1997).

<i>Muscle Group</i>	<i>Test Mode</i>	
	<i>Concentric</i>	<i>Eccentric</i>
Back	-23 (±4)*	-14 (±4)*
Abdomen	-10 (±2)*	-8 (±2)*
Quadriceps	-12 (±3)*	-7 (±3)*
Hamstrings	-6 (±3)*	-1 (±0)*
Tibialis Anterior	-8 (±4)*	-1 (±2)*
Gastroc/Soleus	1 (±3)*	2 (±4)*
Deltoids	1 (±5)*	-2 (±2)*
Pecs/Lats	0 (±5)*	-6 (±2)*
Biceps	6 (±6)*	1 (±2)*
Triceps	0 (±2)*	8 (±6)*